To: Democratic Members of the Government Reform Committee
From: Ranking Minority Member Henry A. Waxman
Re: Summary of FDA Documents
Date: November 17, 2004

On November 4, in response to a request from Chairman Davis and Rep. Waxman, the Food and Drug Administration provided to the Committee more than 1,000 pages of documents relating to FDA's oversight of the Chiron flu vaccine manufacturing facility in Liverpool, England. This is the facility that British regulators shut down on October 5 due to contamination problems, causing the United States to lose approximately half of its supply of flu vaccine.

To assist members in their preparation for the Committee's flu hearing on November 17, 2004, this memorandum reviews the key documents provided by FDA to the Committee.

Executive Summary

The new documents raise serious questions about the adequacy of FDA's oversight. They reveal that despite being aware of major problems at the vaccine manufacturing facility as early as June 2003, FDA missed repeated opportunities to correct them. Specifically, the documents show:

- **FDA found serious and widespread problems at the facility in June 2003.** FDA found problems in 20 areas of vaccine manufacture and distribution, including high levels of bacterial contamination, poor sanitary practices, and inadequate remedial efforts.

- **Problems identified during the June 2003 inspection recurred in 2004 and contributed to the closure of the facility.** The June 2003 inspection identified as significant problems elevated levels of "bioburden" in vaccine pools, contamination by *Serratia* bacteria, deficiencies in the plant's "aseptic connections," improper sanitary practices, and inadequate efforts to investigate and eliminate sources of contamination. These problems recurred in 2004 and were among the factors identified by British, Chiron, and FDA investigators as contributing to the shutdown of the facility. For example, FDA's October 15, 2004, inspection, which confirmed that none of the Chiron

vaccine was safe for U.S. use, cited bioburden problems at the facility that were "not corrected from previous inspection of 2003."

- **FDA officials "downgraded" the agency's response to the June 2003 inspection from "official action indicated" to "voluntary action indicated."** The FDA team that conducted the June 2003 inspection recommended that the agency pursue official enforcement action against the Liverpool facility. But their recommendation that FDA initiate enforcement action was rejected. Instead, FDA requested only voluntary action by the company.

- **FDA delayed sending the final inspection report to the company until June 2004.** When FDA requests voluntary remedial action by a manufacturer, FDA is supposed to send the manufacturer the full inspection report to help the manufacturer understand what corrective actions are needed. In the case of the Chiron facility, FDA did not send the final inspection report to Chiron until June 2004, a year after the inspection occurred and nine months after it was supposed to have been sent. At this point, manufacture of the 2004 vaccine supply was already well underway.

- **FDA never reinspected the plant after June 2003 to determine whether the problems were resolved.** In September 2003, FDA informed the company in writing that the agency would assess the company's corrective actions at its next inspection. This inspection was not scheduled until after the facility was shut down on October 5, 2004, by which time it was too late to save the U.S. flu vaccine supply.

- **FDA remained passive when evidence of actual contamination came to light in August 2004.** After Chiron notified FDA on August 25, 2004, that millions of doses of flu vaccine were contaminated, FDA officials relied on weekly conference calls with Chiron, rather than independent inspections, to monitor the company's progress. These calls included discussion of how FDA officials could dispel fears of a vaccine shortage. By contrast, British regulators launched a series of actions commencing two weeks after receiving the notice from Chiron. These included sending a team of regulators to the facility twice (from September 13 to 15 and from September 28 to 30), reviewing the company's records and draft investigation report, convening two high-level committees, and ultimately suspending the facility's license. FDA officials never asked Chiron or the British regulators about the British activities, and the British regulators were barred by law from informing FDA of their findings absent consent from Chiron.

The Committee staff met with FDA officials on November 15 to discuss the FDA documents. The FDA officials at the meeting, including John Taylor, the Associate Commissioner for Regulatory Affairs, acknowledged that the problems identified during the June 2003 inspection were "relevant" to the contamination in finished lots of vaccine and other systemic concerns that led to the closure of the Chiron plant in October 2004. They also maintained that other factors, such as an increase in the facility's output, played a significant role. The FDA officials justified FDA's failure to take official enforcement action against the facility in June 2003 on the grounds that conditions in the facility appeared to be improving, rather than deteriorating.

The June 2003 Inspection

FDA regulations require that the agency inspect vaccine manufacturers, whether foreign or domestic, at least once every two years.[1] In June 2003, FDA inspected the Liverpool flu vaccine plant of the PowderJect Corporation, which was in the process of being acquired by Chiron.[2] Referring to this inspection, Acting FDA Commissioner Lester Crawford said, "what happened in 2003 has no relevancy for 2004."[3]

In fact, many of the problems detected by FDA during the June 2003 inspection reappeared in 2004 and were among the factors cited as likely or potential causes of the vaccine contamination that led to the closing of the facility this year.

FDA's June 2003 inspection findings are contained in two documents: (1) the Form 483, which is a list of areas of concern that is produced by the FDA inspector during the inspection and is left with the company at the close of the inspection; and (2) the Establishment Inspection Report, which is a detailed description of the findings of the FDA inspection. FDA provided both of these documents to the Committee.

The inspection forms indicate that FDA inspectors found serious problems in 20 areas of vaccine manufacturing and distribution.[4] Several of the problems directly related to the risk of bacterial contamination.

First, the FDA inspectors found high levels of overall bacterial contamination (called "bioburden") in several lots of vaccine after a key step called "ultrafiltration," which is a point in the production process that is supposed to remove the vast majority of bacteria.[5] In some cases, the FDA inspectors found records of bacteria concentrations that were more than a thousand

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[1] 21 CFR 600.21.

[2] PowderJect was formally incorporated into Chiron on October 31, 2003. In purchasing PowderJect, Chiron assumed responsibility for its license to manufacture flu vaccine and its interactions with FDA. Chiron Vaccines, *Chiron Vaccines Expands Presence in UK Following Integration of PowderJect Pharmaceuticals* (Oct. 31, 2003) (online at http://www.powderject.com/company/vaccines_Press_Area_31_October_2003.php).

[3] *Tommy Thompson Holds a News Conference Regarding the Flu*, FDCH Political Transcripts (Oct. 21, 2004).

[4] U.S. Food and Drug Administration, *Inspectional Observations, Form 483, Evans Vaccines Ltd.* (June 10, 2003); U.S. Food and Drug Administration, *Establishment Inspection Report, Evans Vaccines Ltd.* (2003) (hereinafter "Establishment Inspection Report").

[5] Establishment Inspection Report at 13.

times higher than expected.[6] FDA also found evidence of contamination after sterile filtration, the point beyond which there should not be any bacterial growth.[7]

Second, the FDA inspectors found unexpected contamination with potentially lethal bacteria after ultrafiltration. The inspectors determined that on 14 occasions between March 2001 and July 2002, the company found *Serratia* bacteria present in vaccine pools.[8] *Serratia* contamination is a serious problem, because the bacteria can cause abscesses, sepsis, and even death if injected in the human body.

Third, the FDA inspectors identified poor sanitary practices that increased the risk that bacteria could contaminate sterile parts of the production process. For example, the inspectors noted that "curtains" that were supposed to segregate sterile areas of the plant from nonsterile areas were not properly maintained. The inspectors reported:

> [D]uring the June 6th 2003 walk through of the firm's facility it was noted that there was no documentation in the batch record regarding missed stoppers or seals and there is no procedural requirement to do so. Also, a panel about 8 by 10 inches was open in the cabinet under the filling machine and there was no information on the length of time that this condition had existed or that repairs had been scheduled. Furthermore, an operator was noted to be pushing curtains into the area near open empty vials while retrieving tipping vials on 2 occasions disrupting vertical laminar flow and 2 plastic yellow beakers used for holding forceps were observed scratched and yellowed.[9]

One of the most serious problems identified during the June 2003 inspection was that the company did not appropriately investigate and correct possible sources of contamination. For example, the agency learned that the company identified a susceptibility to contamination in the system of connections (called "aseptic connections") between tanks of vaccine in the "Formulation area" of the plant.[10] Yet the FDA inspectors found that the company did not take the appropriate steps to respond to this portal for bacterial contamination. FDA determined that the company's "corrective actions are incomplete."[11]

Similarly, regarding the elevated "bioburden," the inspectors wrote, "there was no documentation that the firm opened a formal investigation into the high levels of bioburden

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[6] *Id.*

[7] Establishment Inspection Report at 15.

[8] FDA also found that 14 vaccine pools had been contaminated by *Klebsiella* bacteria and "several additional batches" by *Enterobacter*. Establishment Inspection Report at 15–16.

[9] *Id.* at 2.

[10] Establishment Inspection Report at 14.

[11] *Id.*

levels to find the root cause and eliminate the potential source/sources of the contamination."[12] The company had also failed to conduct adequate investigations into vaccine sterility and stability issues.[13]

The 2003 inspection also reported that the company sold re-filtered vaccine in the 2001-2002 season without notifying FDA as required by law. Company employees initially told FDA that the re-filtered vaccine was not shipped to the United States. Then the company said that FDA had granted approval to sell re-filtered vaccine. In fact, inspectors determined that neither story was true.[14]

Contrary to Acting Commissioner Crawford's assertion that what happened in 2003 had "no relevancy" to the current flu vaccine shortage, many of the problems that led to the shutdown of the Chiron facility last month were foreshadowed by the June 2003 inspection:

- This year's problems began when Chiron found that several million doses of vaccine had been contaminated with the bacteria *Serratia*.[15] This is the same organism that the FDA inspectors identified as a recurring contamination problem, at an earlier stage in production, in June 2003.[16]

- When British regulators investigated the 2004 *Serratia* contamination, they discovered several months of abnormally high levels of bioburden in vaccine pools and determined that the company had failed to understand what was causing these high levels.[17] These concerns were similar to those identified by the FDA inspectors in June 2003.[18] When FDA investigators finally visited the plant in October 2004, they found that bioburden problems were "not corrected from previous inspection of 2003 in that similar occurrences noted during this inspection."[19]

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[12]Establishment Inspection Report at 2.

[13]Establishment Inspection Report at 12 and 14.

[14]Establishment Inspection Report at 9–10.

[15]*Half of U.S. Flu Vaccine Withheld*, Washington Post (Oct. 6, 2004) ("In August, Chiron told that agency it had found some lots of vaccine contaminated with *Serratia***,** a genus of 'gram-negative' bacteria that can cause severe, and occasionally fatal, infections in human beings").

[16]Establishment Inspection Report at 16.

[17]Medicines and Healthcare Products Regulatory Agency, *2004 Fluvirin Manufacturing Campaign — Inspectorate Findings* (Oct. 4, 2004).

[18]Establishment Inspection Report at 13.

[19]U.S. Food and Drug Administration, *Inspectional Observations, Form 483, Evans Vaccines, an Affiliate of Chiron Corporation*, 6 (Oct. 15, 2004).

- When Chiron investigated the August 2004 *Serratia* contamination, the company determined that the bacteria could have entered the vaccine through aseptic connections between tanks in the formulation area of the plant.[20] An FDA official also wrote in an internal agency memo that the Serratia contamination was most likely to have occurred through these connections between tanks involved in formulation.[21] This is same part of the production process that the FDA inspectors reported had not been adequately investigated and corrected in June 2003.[22]

- In reviewing possible sources of the 2004 *Serratia* contamination, Chiron found damage to the flooring, a skipped monthly cleaning in June 2004, and an employee whose training in aseptic technique had lapsed. While Chiron did not consider any of these specific problems to be the cause of this year's vaccine problems, the company considered it probable that bacteria had inadvertently been passed from nonsterile areas to sterile areas of the production process.[23] In October 2004, FDA inspectors again identified problems in the handling of curtains separating sterile from nonsterile areas and other sanitary practices at the plant.[24] FDA inspectors had expressed concern about the consequences of such problems in June 2003.[25]

- FDA and British regulators concluded in October 2004 that Chiron had failed to investigate the contamination problems effectively.[26] Difficulty pursuing such investigations was a recurring theme of the June 2003 inspection.[27]

The FDA officials who briefed the Committee on November 15 were asked whether the problems identified during the June 2003 inspection were related to the problems that led to the closure of the facility in October 2004. They acknowledged that a number of the problems found during the June 2003 inspection were the same as or related to problems found in 2004. They emphasized, however, that the problems found in 2004 were worse and more widespread than in

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[20]Chiron Vaccines, *Fluvirin Sterility Investigation*, 39–46 and 66–67 (2004).

[21]Angela K. Shen, U.S. Food and Drug Administration, *Status of 2004 Flu Campaign* (Sept. 2, 2004).

[22]Establishment Inspection Report at 14.

[23]Chiron Vaccines, *supra* note 20, at 39–46.

[24]U.S. Food and Drug Administration, *supra* note 19.

[25]Establishment Inspection Report at 24–25.

[26]Medicines and Healthcare Products Regulatory Agency, *supra* note 17; U.S. Food and Drug Administration, *supra* note 19.

[27]U.S. Food and Drug Administration, *Inspectional Observations, Form 483, Evans Vaccines Ltd.* (June 10, 2003).

2003. In their view, the effort to increase the output of the Chiron plant in 2004 contributed significantly to the deterioration in the conditions.[28]

FDA's Response to the June 2003 Inspection

The June 2003 inspection report and Form 483 could have served as a road map for stringent enforcement and oversight on FDA's part. However, the agency missed opportunities to ensure that the problems would be fixed and the public would be protected.

In a previous inspection in 1999, FDA inspectors identified problems at the Liverpool facility. The inspectors responded to these problems by issuing an FDA "warning letter."[29] This is an official enforcement action that is released to the public. If the manufacturer does not remedy the violations identified in the warning letter, FDA can initiate legal action against the manufacturer. In addition, a warning letter generally ensures that another inspection will be conducted to assess whether compliance has been achieved.

After the June 2003 inspection, however, FDA failed to initiate any official enforcement action. Although FDA inspectors recommended official enforcement action, this recommendation was rejected. The October 5 handwritten notes of John Eltermann, the director of the Division of Manufacturing and Product Quality in FDA's Center for Biologics, Evaluation and Research under the heading of June 2003 state: "TBio – OAI → VAI." There is a single word underneath: "downgraded."[30]

FDA officials were asked about the significance of these notes at the November 15 briefing. The FDA officials explained that the abbreviation "TBio" refers to "team biologics," the FDA unit responsible for inspecting vaccine manufacturers, the abbreviation "OAI" refers to "official action indicated," and the abbreviation "VAI" refers to "voluntary action indicated." According to the FDA officials, the "team biologics" inspectors, who conducted the June 2003 inspection, recommended that the agency pursue official enforcement action against the Liverpool facility. But this recommendation was not accepted. Instead, it was "downgraded" to a request for voluntary action by the company, which carries no legal weight.[31]

According to the FDA officials, the decision to "downgrade" the enforcement action was primarily justified by the quality of the company's plan to fix the problems and by improvement in bacterial contamination noted during the 2002 to 2003 flu season. The June 2003 inspection

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[28]U.S. Food and Drug Administration, Briefing for Government Reform Committee staff (Nov. 15, 2004).

[29]Warning letter from Steven A. Masiello, Director, Office of Compliance and Biologics Quality, Center for Biologics Evaluation and Research, U.S. Food and Drug Administration, to Mr. John E. O'Brian, Head of Primary Production, Medeva Pharma Ltd. (Oct. 21, 1999).

[30]John Eltermann, U.S. Food and Drug Administration, *Notes of Internal FDA Discussions* (Oct. 5, 2004).

[31]U.S. Food and Drug Administration, *supra* note 28.

report found 20 deficiencies at the plant compared to 31 in the 2001 inspection. According to the 2003 inspection report, 26 of the problems identified in the 2001 inspection had been corrected. Five deficiencies remained uncorrected.[32]

Acting FDA Commissioner Crawford has assured the public that the agency did provide adequate oversight of the vaccine facility after the June 2003 inspection. Responding to a question about whether Chiron had implemented necessary corrective actions after the June 2003 inspection, Dr. Crawford stated: "We monitored those actions. Those actions were taken."[33]

In fact, the documents indicate otherwise. During the 16 months between the June 2003 inspection and the October 2004 shutdown of the facility, FDA failed to inspect — even once — whether the manufacturing defects it identified in June 2003 had been fixed. FDA informed the company that "corrective actions will be reviewed and assessed during the next inspection."[34] But such an inspection did not occur until mid-October 2004, after British regulators had shut down the facility. By then, it was too late to prevent the flu vaccine shortage.[35]

FDA also failed to respond to the company's requests for assistance. On June 27, 2003, the plant's manager wrote to FDA that the company "would like to meet with the agency as soon as possible" to review its response plan. He stated, "At this meeting we would welcome the opportunity to present to the agency our Quality Systems Improvements Program."[36] FDA replied to Chiron over two months later, on September 3, 2003. The response states that the company's letter would be placed in its "permanent file."[37] No mention was made of the meeting request, and according to Chiron officials, no meeting ever occurred.[38] When asked during the November 15 congressional briefing about the failure of FDA to meet with Chiron, the FDA officials stated that the agency often declines to meet with companies that have presented adequate plans for addressing inspection problems.[39]

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[32]Establishment Inspection Report at 5–6.

[33]*Tommy Thompson Holds a News Conference Regarding the Flu*, *supra* note 3.

[34]Letter from Philip R. Lindeman, Compliance Officer, U.S. Food and Drug Administration, to Mr. Andy Sneddon, Site Manager, Evans Vaccines, Ltd. (Sept. 3, 2003).

[35]U.S. Food and Drug Administration, *FDA Team Completes Inspection of Chiron's Liverpool Flu Vaccine Plant* (Oct. 15, 2004) (online at http://www.fda.gov/bbs/topics/news/2004/NEW01125.html).

[36]Letter from Mr. A.H. Sneddon, Site Director, Evans Vaccines, Ltd., to K. Midthun, Center for Biologics Evaluation & Research, U.S. Food and Drug Administration (Jun. 27, 2003).

[37]Letter from Philip R. Lindeman, *supra* note 34.

[38]Chiron Corporation, Briefing for Chairman Davis and Government Reform Committee staff (Nov. 11, 2004).

[39]U.S. Food and Drug Administration, *supra* note 28.

One problem acknowledged by the FDA officials at the November 15 briefing was the long delay in providing the final inspection report to Chiron. On June 7, 2004 — a year after the completion of the June 2003 inspection — Chiron officials wrote FDA to request a copy of the Establishment Inspection Report from the June 2003 visit.[40] This report contains many more details and recommendations than the Form 483. According to FDA staff, this report should have been sent to the facility in September 2003, when the decision was made to request only voluntary action, in order to assist the plant in taking the appropriate remedial steps. In fact, the report was not provided until after FDA received Chiron's June 7, 2004, request, well after the start of vaccine manufacturing for the 2004 to 2005 season.[41] According to FDA officials, confusion between FDA's Center on Biologics, Evaluation and Research and the Office of Regulatory Affairs was responsible for the delay.[42]

FDA's Response to the August 2004 Contamination

FDA had another opportunity to intervene in August 2004, when Chiron reported that it had detected contaminated vaccine at the Liverpool facility. On August 26, 2004, Chiron announced that eight lots of vaccine, representing several million doses, had been contaminated by *Serratia*.[43] The documents indicate, however, that FDA failed to act decisively.

Acting Commissioner Crawford has characterized the British and FDA inspections in response to the August announcement as "about the same thing" and said that the two countries' drug agencies were "in synchrony."[44] But the documents do not support these assertions. Even though none of the vaccine contaminated in August was intended for the British market, and even though the United Kingdom relied on the Chiron plant for a small fraction of its overall flu vaccine supply, British regulators did far more than their FDA counterparts to ensure the safety of the flu vaccine.

When Chiron notified FDA of the *Serratia* contamination on August 25, an agency inspector coincidentally was present at the facility conducting a limited inspection of a new filling line for vaccine. Chiron asked to brief this inspector about the company's investigation into the problem. According to his notes, this inspector learned basic details about the

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[40]Letter from Peter McBride, Regulatory Affairs Managers at Evans Vaccine Limited (part of Chiron Vaccines) to Dr. James S. Cohen, Office of Compliance and Biologics Quality, Food and Drug Administration (Jun. 7, 2004).

[41]U.S. Food and Drug Administration, *supra* note 28.

[42]U.S. Food and Drug Administration, *supra* note 28.

[43]Chiron Corporation, *Chiron Delays Fluvirin(R) Influenza Virus Vaccine Shipments* (Aug. 26, 2004) (online at http://www.chiron.com/media/pressreleases/index.html).

[44]*Tommy Thompson Holds a News Conference Regarding the Flu*, *supra* note 3.

contamination of eight lots of the vaccine and heard of the company's plans to "continue to identify root cause."[45]

From this point on, however, FDA relied on conference calls with the company — not its own inspections or review of company records — to monitor the company's progress.

According to internal agency notes and e-mails, these conference calls would include an update from Chiron on the company's findings, combined with a discussion about how to handle the public relations problems created by the August announcement. On September 9, for example, FDA and Chiron discussed the media coverage of the *Serratia* contamination and considered a plan to "dispel fears of shortages, and to state that, overall, more vaccine is expected to be available this season than last year."[46]

Even when asked by the company for more active oversight of the *Serratia* investigation, FDA remained passive. On September 20, a senior Chiron official asked whether the agency had any "special issues" for the company to act upon before going forward. In response, an FDA official said that he did not think so, "provided they are following SOPs [standard operating procedures], the product meets specifications and they believe that they have isolated and resolved the issue."[47]

Internal e-mails indicate that even in late September, FDA employees tried to dispel rumors of a pending shortage. For example, FDA officials spoke on September 20 with a senior official at the National Vaccine Program Office of the Department of Health and Human Services to alleviate heightened concerns about the Chiron situation.[48]

By contrast, upon learning of *Serratia* contamination, Britain's Medicine and Healthcare products Regulatory Agency (MHRA) — the British equivalent of FDA — took a different approach. Within two weeks, the agency sent a team of inspectors to the facility to conduct a two-day "fact finding" visit to the plant on September 13 and 14, 2004.[49] Reviewing the company's records, the British inspectors found that Chiron knew of potential contamination

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[45]U.S. Food and Drug Administration Inspector David Cho, *Notes from Discussion with Chiron/Evans on 25 August 2004* (Aug. 25, 2004).

[46]E-mail communication from Elaine Cole, U.S. Food and Drug Administration, to other FDA employees, *Conference Call Summary — Chiron's Fluvirin* (Sept. 9, 2004).

[47]E-mail communication from Roland A. Levandowski, U.S. Food and Drug Administration, to other FDA employees, *Evans/Chiron Update* (Sept. 20, 2004).

[48]E-mail communication from Roland A. Levandowski, U.S. Food and Drug Administration, to other FDA employees, *RE: Evans/Chiron Update* (Sept. 20, 2004).

[49]Medicines and Healthcare Products Regulatory Agency, *Briefing Note: Chiron Vaccines, Speke, Liverpool, Influenza Vaccine*, 1 (Oct. 5, 2004).

problems as early as April 2004.[50] They also learned that sterility failures occurred in July 2004.[51]

On September 15, MHRA convened the Cross-Agency Vaccine Group to review the inspectors' report.[52] This high-level panel advised that a second visit should take place after a review of the company's draft internal investigation of the *Serratia* contamination.[53]

This draft was provided by Chiron on September 24. It was immediately reviewed by senior British regulators, including the Acting Director of MHRA's Inspection and Enforcement Division.[54] While FDA officials never received this draft report from the company, the British officials quickly determined that the report "had not addressed the root causes of the contamination problems."[55]

In response, the British arranged for a second "for cause" inspection to take place from September 28 to 30.[56] MHRA also requested, in writing, that Chiron not release "any batches of vaccine to any market pending that visit."[57]

After the inspection from September 28 to 30, MHRA's Cross-Agency Vaccine Group met again on October 1. At this meeting, inspectors identified 19 "serious issues related to microbial contamination and potential for microbial contamination in influenza vaccine production."[58] According to the inspectors, "these constituted a critical situation regarding sterility assurance of the production process, leading to potential and actual microbial contamination of the finished product by a pathogenic organism."[59]

The Cross-Agency Vaccine Group referred the report to MHRA's Inspection Action Group, which recommends licensing actions.[60] This panel met on October 4 and recommended

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[50] *Id.*

[51] *Id.*

[52] *Id.*

[53] *Id.*

[54] *Id.*

[55] *Id.*

[56] *Id.*

[57] *Id.*

[58] *Id.* at 2.

[59] *Id.*

[60] *Id.*

the suspension of Chiron's license to prevent "a potentially serious risk to patients through the administration of a vaccine that may be contaminated."[61] The closure of the Chiron facility by the British was announced the following day, on October 5.

FDA officials were caught completely unaware by these British actions. In fact, FDA officials did not even know that British regulators were investigating the Chiron facility until October 5, after the facility was shut down. At the November 15 briefing, FDA officials acknowledged that FDA never asked Chiron or the British regulators about the activities of the MHRA.[62] For their part, the British regulators did not tell FDA officials about their efforts because they were prevented by law from telling FDA of their activities without the consent of Chiron.

After MHRA's public announcement of the plant's shutdown on October 5, FDA finally conducted an on-site inspection of the Chiron facility which ended on October 15. This inspection confirmed that "none of the influenza vaccine manufactured by the Chiron Corporation for the U.S. market is safe for use."[63]

At the November 15 briefing, FDA officials stated that the agency was planning to review the company's inspection report during the week of October 5. According to these officials, FDA would have immediately recognized the deficiencies in the Chiron report and scheduled a rapid inspection. Yet even if FDA had acted immediately, the earliest that FDA could have suspended the company's license would have been after the October 15 inspection. During this delay, additional millions of flu shots from the other manufacturer serving the U.S. market might have been administered to low-risk individuals around the country, worsening the shortage to come.

After the License Suspension

After British regulators suspended Chiron's license to manufacture and market flu vaccine on October 5, 2004, FDA was unclear on how to proceed. Letters from the Office of the General Counsel at FDA to MHRA indicate that the agency did not understand the reach or implications of the British decision. An e-mail to MHRA from the associate chief counsel for biologics asked "for a copy of the law or regulation which provides the licensing authority in the United Kingdom with the power to order the suspension."[64] FDA also asked to learn whether Chiron had any remedies for the administrative action, whether the company could ask for retesting of batches or lots, and whether the suspension order affected lots located in the United States.[65]

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[61] *Id.*

[62] U.S. Food and Drug Administration, *supra* note 28.

[63] U.S. Food and Drug Administration, *supra* note 35.

[64] E-mail communication from Office of General Counsel, U.S. Food and Drug Administration, to MHRA, *Questions Regarding the Suspension* (Oct. 6, 2004).

[65] *Id.*

Conclusion

In sum, the documents from FDA disclose that the agency failed to provide effective oversight of the Liverpool facility. Despite identifying serious problems at the facility in June 2003, FDA failed to take official enforcement action or to conduct followup inspections. Even after being told in August 2004 of additional contamination, FDA did little to determine the true scope of the problems. If FDA had acted differently — by issuing an official warning letter, reinspecting the facility, and responding aggressively to the August 2004 contamination — the flu vaccine shortage might have been avoided or mitigated.